Not so Kind(lin) on the intestine

Mutations in the gene that encodes the Kindlin-1 protein are responsible for the rare, recessive genodermatosis Kindler syndrome (KS). Kindlin-1 is an epithelial cell adaptor protein and localizes to cell–matrix adhesion sites to regulate integrin function. Although skin and oral mucosa abnormalities have been associated with KS, some patients have also developed ulcerative colitis. To probe these associations, Ussar and colleagues generated mice carrying a constitutive null mutation in the Kindlin-1 gene. The mice exhibited skin atrophy and reduced keratinocyte proliferation, similar to that observed in KS patients. In addition, the mutant mice died shortly after birth (P3–P5) as a result of intestinal epithelial dysfunction caused by loss of the intestinal epithelial barrier and subsequent inflammatory cell infiltrate. Loss of Kindlin-1 impaired integrin activation and thus compromised adhesion of colonic epithelial cells. Future therapeutic strategies for KS treatment that involve rerouting the related Kindlin-2 protein to integrin adhesion sites may prove useful. (*PLoS Genet*, published online 5 December 2008; doi:10.1371/journal.pgen.1000289)

One step in the atopic march

Because atopic dermatitis (AD) often precedes the development of other atopic disorders such as asthma and allergic rhinitis, it may be considered the initial step in the "atopic march." Expression of thymic stromal lymphopoietin (TSLP) in keratinocytes is necessary and sufficient to trigger AD inflammation. Zhang and colleagues employed a mouse model of ovalbumin (OVA)-induced asthma to determine whether TSLP-induced AD is associated with asthma occurrence. Following induction of AD with MC903 (calcipotriol), mice exposed to the OVA experimental asthma protocol exhibited TSLP induction in keratinocytes, AD-like skin inflammation, and an aggravated allergenic asthmatic phenotype. TSLP production by keratinocytes was necessary for this aggravation of OVA-induced asthma following MC903 treatment. Interestingly, epidermal TSLP production during the allergen sensitization period aggravated allergic inflammation in the airway, despite the fact that the AD had resolved and TSLP levels were again normal at the time of allergen challenge. Thus, overproduction of TSLP in AD patients' skin may be viewed as a risk factor for allergic airway inflammation. (*Proc Natl Acad Sci USA* 106:1536–41, 2009)

Regulating desmosomes and differentiation

Kazrin, which binds the cornified envelope protein periplakin, has been suggested to function in the interplay between desmosomes and adherens junctions. Sevilla and colleagues demonstrated that overexpression of kazrin, which is typically upregulated during keratinocyte differentiation, led to profound changes reminiscent of cells undergoing terminal differentiation, including alterations in cell shape, spreading, and stretching. In fact, kazrin overexpression resulted in reduced clonal growth, increased size and granularity, and increased expression of the terminal differentiation markers involucrin and transglutaminase 1, supporting an increase in keratinocyte terminal differentiation. Furthermore, overexpression of kazrin inhibited desmosome assembly and Rho GTPase activity, which is critical for the regulation of the cytoskeleton and cell–cell adhesion. Together, these data support a role for kazrin in the regulation of desmosome assembly through the inhibition of Rho and the stimulation of differentiation via a Rho-independent pathway. (*J Cell Sci* 121:3561–9, 2008)

Tanning for kids

Although the vast majority of US adolescents are aware of the dangerous effects of UVR, many continue to use indoor tanning facilities. During a recent meta-analysis of data collected by the American Cancer Society in 1998 and 2004, Cokkinides and colleagues discovered that the prevalence of indoor tanning use in adolescents aged 11–18 did not change significantly during this time period (10% to 11%), despite legislation by states to restrict minors' access to tanning without parental consent. In agreement with previous studies, parental permission was correlated with higher indoor tanning use by adolescents. In addition, 57.5% of the interviewed adolescent users reported getting red or burned from these tanning devices. Given the known health risks of early UVR exposure from the sun or indoor tanning facilities, a multipronged approach involving stricter legislation and parent and adolescent education is clearly warranted to decrease the use of these devices by adolescents. (*Cancer* 115:190–8, 2009)

Dermatologist density predicts melanoma prognosis

Researchers have posited that physician density may influence cancer prognosis. Survival disparities persist among sociodemographic groups, and these differences may be explained, in part, by racial heterogeneity and varying levels of education, household income, and access to health care. Eide and colleagues perused melanoma cancer registry data from the National Cancer Institute SEER (Surveillance, Epidemiology, and End Results) program, as well as additional data sources for provider specialty and density, to examine the associations between dermatologist density and melanoma outcomes. Density and specialty of physicians were significant predictors of melanoma prognosis regardless of patients' socioeconomic status. Indeed, melanoma patients who reside in counties with more dermatologists have better prognostic outcomes. This report underscores the efforts to recruit physicians—particularly specialty physicians, such as dermatologists—to underserved communities, which may be rural or highly dense urban communities. (*J Am Acad Dermatol* 60:51–8, 2009)

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